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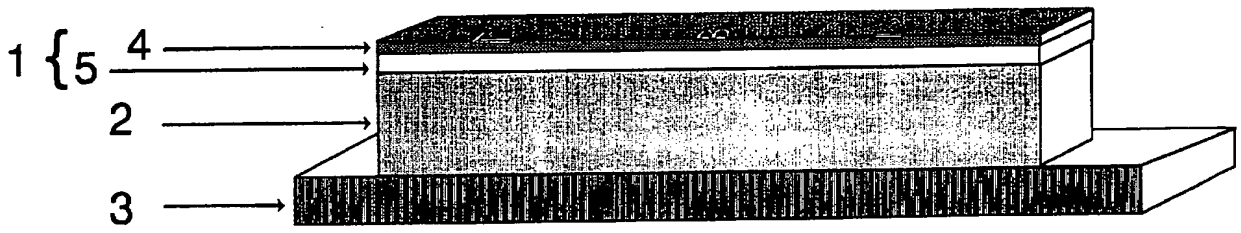
(72) Inventeurs/Inventors:
HORSTMANN, MICHAEL, DE;
STEINBORN, PETER, DE

(73) Propriétaire/Owner:
LTS LOHMANN THERAPIE-SYSTEME AG, DE

(74) Agent: BLAKE, CASSELS & GRAYDON LLP

(54) Titre : SYSTEME THERAPEUTIQUE TRANSDERMIQUE A IDENTIFICATION EXEMPTE D'ENCRES D'IMPRIMERIE ET SON PROCEDE DE FABRICATION

(54) Title: TRANSDERMAL THERAPEUTIC SYSTEM IDENTIFIED WITHOUT PRINTING INKS AND PROCESS FOR MANUFACTURING THE SAME



(57) Abrégé/Abstract:
A transdermal therapeutic system is disclosed to administer active substances through the skin to the human body. The backing layer consists of pharmaceutically usual plastic foil laminates made of thermoplastic materials that melt at a low temperature on its outer side and of thermoplastic materials that melt at a higher temperature facing the skin. The backing layer needs to be identified, for example by printing. Using pigments or lacquers for printing creates problems, however, because of their toxicological and technological inconvenients, as well as legal restrictions that apply to medicaments. According to the invention, therefore, the identification code does not consist of a dye or pigment layer, but of a modification of the surface structure of the backing layer that corresponds to the identification code.

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(71)(72) Anmelder und Erfinder: HORSTMANN, Michael [DE/DE]; Fürst-Friedrich-Karl-Strasse 9, D-56564 Neuwied (DE).

(72) Erfinder; und
(75) Erfinder/Anmelder *(nur für US)*: STEINBORN, Peter [DE/DE]; Aubisch 20, D-56567 Neuwied (DE).

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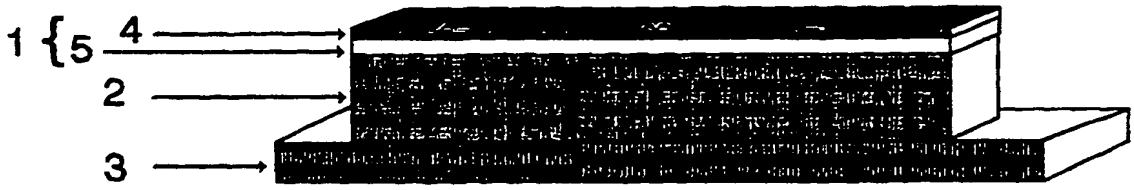
(54) Title: TRANSDERMAL THERAPEUTIC SYSTEM IDENTIFIED WITHOUT PRINTING INKS AND PROCESS FOR MANUFACTURING THE SAME

(54) Bezeichnung: TRANSDERMALES THERAPEUTISCHES SYSTEM MIT DRUCKFARBENFREIER IDENTIFIKATION UND VERFAHREN ZU SEINER HERSTELLUNG



(57) Abstract

A transdermal therapeutic system is disclosed to administer active substances through the skin to the human body. The backing layer consists of pharmaceutically usual plastic foil laminates made of thermoplastic materials that melt at a low temperature on its outer side and of thermoplastic materials that melt at a higher temperature facing the skin. The backing layer needs to be identified, for example by printing. Using pigments or lacquers for printing creates problems, however, because of their toxicological and technological inconvenients, as well as legal restrictions that apply to medicaments. According to the invention, therefore, the identification code does not consist of a dye or pigment layer, but of a modification of the surface structure of the backing layer that corresponds to the identification code.

(57) Zusammenfassung

Die Erfindung betrifft ein Transdermales Therapeutisches System zur Abgabe von Wirkstoffen über die Haut an den menschlichen Körper. Die Rückschicht besteht aus pharmazeutisch üblichen Kunststoffolienlaminaten aus einem außenseitig liegenden bei niedriger Temperatur schmelzenden Thermoplasten und einem zur Haut hin gewandten, höher schmelzenden Thermoplasten, welche eine Kennzeichnung, zum Beispiel durch Bedruckung benötigt. Die Problemstellung beruht auf toxikologischen, technologischen und arzneimittelrechtlichen Nachteilen einer Pigment- oder Lackbedruckung. Die Codierung besteht erfindungsgemäß nicht in einer Farb- oder Pigmentschicht, sondern durch eine dem Code entsprechende Beeinflussung der Oberflächenbeschaffenheit der Rückschicht.

Transdermal therapeutic system with inkless identification and method for its manufacture

Description

The invention relates to a transdermal therapeutic system delivering active agents to the human body through the skin.
Transdermal therapeutic systems are introduced already in the market for pharmaceutical treatment of a number of diseases and have proved themselves therefore in practice.
Moreover, a number of different possible system designs are known from the literature (see for example Y.W. Chien in: A.F. Kydonieus and B. Berner (eds.) "Transdermal Delivery Of Drugs", p. 81-100).
There is some fundamental similarity however also independently of this variety of possible system designs between the systems known at the time being:
1. For protection against unwanted delivery of active agent or also skin moisture by the transdermal therapeutic system and also for protection against adhesion to textiles, an essentially impermeable, not sticking backing layer (1) is used.
2. As transdermal therapeutic systems have to stick on the skin, the layer facing the skin, occasionally only a part of the area is made pressure-sensitive adhesive.
3. Because of these self-adhesive qualities, a removable protective layer (3) made dehesive, if necessary is added for storage purposes before use.

The backing layer consists of usual pharmaceutical materials like plastic webs, but also papers, nonwovens or textiles may apply. Frequently, thermoplastic plastics are used because of their easy processability, so as e.g. extruded or cast, stretched e.g. along the length or cross, films or also in form of fibers in

their use as non-woven-like or textile applications.
Specifically suited plastics are exemplary polyethylene terephthalate (PETP) and other polyesters, polyethylene (HDPE or LDPE), polyvinyl chloride (PVC, optional softenized), ethylene-vinyl acetate-copolymers (EVA) and polypropylene (PP). In order to combine the combination of advantageous features, also laminates are in use (for example such from EVA or PE (outer surface) and PETP). The surface (4) can this way (PE or EVA) be equipped with skin-like soft "touch" and on the other side, a PETP layer (5) may act as a diffusion barrier against the active part of the transdermal therapeutic system.

Similarly as in case of conventional pharmaceutical forms of application, the marketing companies, the regulatory agencies or generally consumer organizations wish or even make the obligation to a clear identification of those systems. In this way, a sure identification of the product shall this way be possible if package leaflet and other accompanying information is not available. Form, size and appearance alone cannot make sure this alone.

It has become therefore usual in the meantime to print such systems with a suitable printing ink on the outside of the backing layer. This possibility, described in EP 0 114 125, allows already identification and makes coloured noticeable features possible.

Furthermore, it is known in general plastics that thermoplastic plastics are deformable in the heat and this change of shape may be utilized to emboss patterns or information on everyday commodities, also on plastic laminates (see e.g. US 4 359 442).
For labeling of articles, in special also the packing of pharmaceutical products, however, only transfer printing is usual at which a pigmented plastic laminate is pressed shortly against the matter to be printed. This way ink pigment is applied onto the substrate.

Also embossing is known in principle as a procedure to label transdermal therapeutic systems (DE-Gbm 94 9 784). Here, sheet-like means of labeling with embossments or prints are applied on the drug-containing part of patches containing pharmaceutical agents.

This state of the art is nevertheless connected with a number of disadvantages:
- with the use of (only toxicologically acceptable) printing inks, to work with solvent-containing carrier fluids for pigments and varnishes at the place of the manufacture of pharmaceutical products is not unproblematic because of possible contamination with foreign materials.
A number of varnishes does not or only insufficiently stick on the backing material; this way only printable materials are suitable.
The printing ink on the transdermal therapeutic systems may soften during storage and the imprint become unreadable upon the influence of volatile agents.
Furthermore, a color print code on the transdermal therapeutic system is disturbing cosmetically for the consumer.

- If, like in DE-Gbm 94 9 784, embossing is chosen for application of the coding, at application of ordinary techniques accessible for the expert, the drug-containing part has to be exposed to an undue and high pressure, noxious for the pharmaceutical form of application.
Compression of the matrix this way easily leads to local changes of the function of the patch, particularly the release in vitro. An embossment performed prior to application of a sheet-like carrier of label requires a second pressure sensitive adhesive intermediate layer and nearly necessarily leads to a bubble-containing unattractive appearance.
The embossment mentioned in DE-Gbm 94 09 784 is not described technically more precisely in the detail there. At use of a (by far predominantly used) backing made of an uniform polymer material, an embossment, in any way

performed, with or without the action of heat, is connected with the production of of "thin areas". This may destroy the barrier property of the backing for the active agent and is obviously for this reason not done in practice.

The task of the present invention is therefore a transdermal therapeutic system consisting of a backing layer of thermoplastic material consisting of a laminate of a low-melting thermoplastic material on the external surface and a higher melting thermoplastic material facing the skin side, and a persistent, identifying code applied on this laminate, as well as an active part containing the active agent, which allows a safe labeling on said backing layer without the use of further additives.
According to this invention, the task is settled by the fact that this coding consists of a locally different surface property, surface thickness or surface roughness.

The advantages of the matter of invention are observed particularly with active agents or also other ingredients which are volatile at the storage temperature provided and therefore may migrate through the gas space into materials according to state of the art.

Such substances are nicotine, nitroglycerine, for example as examples for pharmaceutical agents. Ethanol, propylene glycol and other low molecular alcohols, menthol, eucalyptol, limonene and many other terpenes, low molecular fatty acids such as capric acid and dimethyl sulfoxide are named exemplarily as typical additives in transdermal therapeutic systems for typical excipients which represent a risk factor for classical printing technology. Surprisingly not, as to be expected by the expert, a disadvantageous change of drug content occurs upon the influence of temperature.
Particularly by application of modern printing tools and machinery, impairment of drug content is practically excluded at short contact times.

The invention is represented in Fig. 1 in detail. Instead of the diffusion matrix (2) shown, also other typical elements of such pharmaceutical forms of application and element groups (reservoirs, diffusion membranes, etc.) may be used without impairing the inventive solution.

Fig. 1 shows a transdermal therapeutic system in cross-section with backing layer (1) divided up into printable thermoplastic layer (4) and diffusion-(and temperature-) barrier (5).
It contains therefore the elements:

1	Backing layer, consisting of (4) and (5), with coding
2	Matrix
3	Removable protecting layer
4	Thermoplastic part of the backing layer with imprint
5	Diffusion barrier for the active agent (PETP)

Claims:

1. Transdermal therapeutic system, with backing layer of thermoplastic material, consisting of a laminate of a low-melting thermoplastic material on the external surface and a higher melting thermoplastic material facing the skin side, and a persistent, identifying code applied on this laminate, as well as an active part containing an active agent, characterized in that this coding consists of a locally different surface property, surface thickness or surface roughness of this backing layer.

2. Transdermal therapeutic system according to claim 1, characterized in that this coding is generated by influence of pressure, heat, ultrasound or abrasion.

3. A transdermal therapeutic system comprising a backing layer and an active agent containing matrix layer, wherein the backing layer is provided with persistent information which consists of a coding formed by a locally different surface property, surface thickness or surface roughness of the backing layer, said backing layer consists of a laminate comprising an external layer and a layer facing the matrix, wherein the external layer is a low-melting thermoplastic material containing said information and the layer facing the skin is a higher melting thermoplastic material which protects the active agent containing matrix layer from damage during coding.

4. A method for manufacturing the transdermal therapeutic system according to claim 1 or 3 wherein the coding is performed after the completion of a process for preparing the transdermal therapeutic system, said coding is accomplished by the influence of pressure, heat, ultrasound or abrasion.

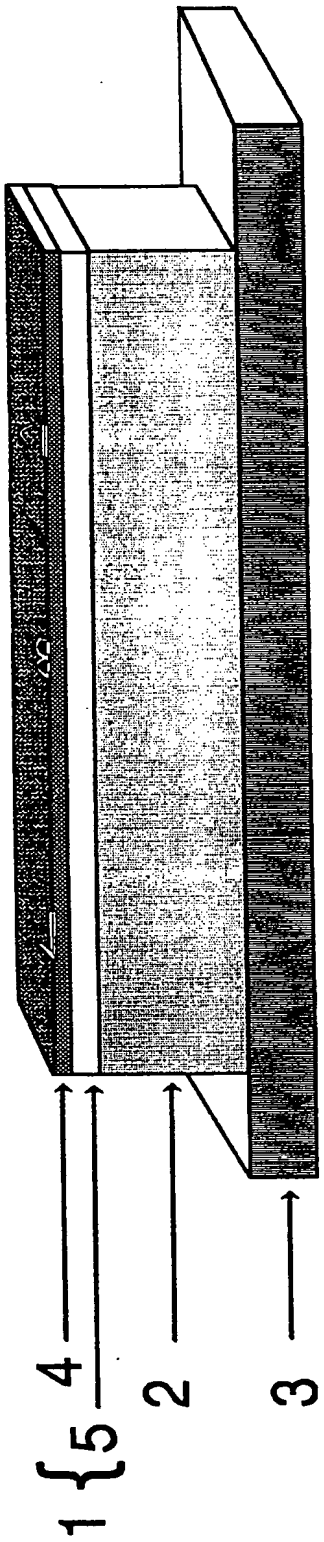


Fig. 1:

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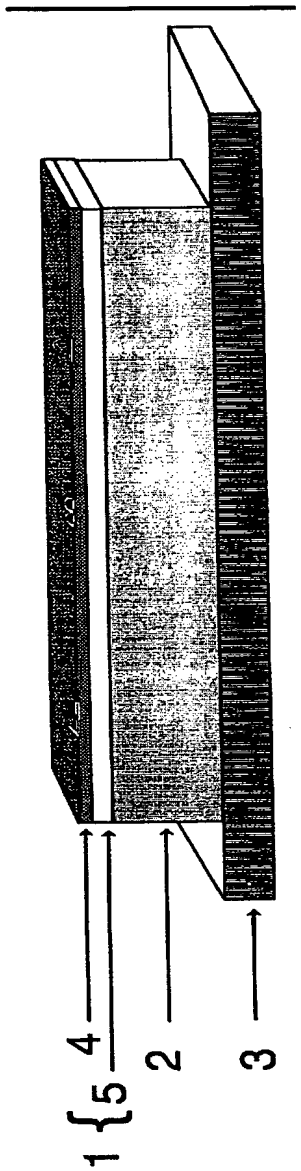
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